

Title: METHODS FOR THE PRODUCTION OF REDOX  
PROTEINS.

Applicant: van Rooijen et al.

Serial No. 10/032,201 Filed: December 19, 2001

Our Docket No.: 38814-351B

10 20 30 40 50 60  
TR ATGAATGGTCTCGAAACTCACAACACAAGGCTCTGTATCGTAGGAAGTGGCCAGCGGCA  
ATTHIREDB ATGAATGGTCTCGAAACTCACAACACAAGGCTCTGTATCGTAGGAAGTGGCCAGCGGCA

70 80 90 100 110 120  
TR CACACGGCGGCGATTACGCAGCTAGGGCTGAACCTTAAACCTCTTCTCTTCGAAGGATGG  
ATTHIREDB CACACGGCGGCGATTACGCAGCTAGGGCTGAACCTTAAACCTCTTCTCTTCGAAGGATGG

130 140 150 160 170 180  
TR ATGGCTAACGACATCGCTCCCGGTGGTCAACTAA[CAACCA]C[C]A[C]GAGCTGAGAATTTCT  
ATTHIREDB ATGGCTAACGACATCGCTCCCGGTGGTCAACT--[CAACCA]A[C]A[C]GAGCTGAGAATTTCT

190 200 210 220 230 240  
TR CCCGGATTTTCAGAAAGGTATTCTCGGAGTAGAGCTCACTGACAAATTCGGTAAACAATCG  
ATTHIREDB CCCGGATTTTCAGAAAGGTATTCTCGGAGTAGAGCTCACTGACAAATTCGGTAAACAATCG

250 260 270 280 290 300  
TR GAGCGATTTCGGTACTACGATATTTACAGAGACGGTGACGAAAGTCGATTCTCTTCGAAA  
ATTHIREDB GAGCGATTTCGGTACTACGATATTTACAGAGACGGTGACGAAAGTCGATTCTCTTCGAAA

310 320 330 340 350 360  
TR CCGTTTTAAGCTATTACAGATTTCAAAGCCATTCTCGCTGACGCTGTGATTCTCTCGCTATC  
ATTHIREDB CCGTTTTAAGCTATTACAGATTTCAAAGCCATTCTCGCTGACGCTGTGATTCTCTCGCTATC

370 380 390 400 410 420  
TR GGAGCTGTGGCTAAGTGGCTTAGCTTCGTTGGATCTGGTGAAAGGTTCTGGAGGTTTCTGG  
ATTHIREDB GGAGCTGTGGCTAAGTGGCTTAGCTTCGTTGGATCTGGTGAAAGGTTCTGGAGGTTTCTGG

430 440 450 460 470 480  
TR AACCGTGGAATCTCCGCTTGTGCTGTTTGGCAGCGAGCTGCTCCGATATTCGGTAAACAAA  
ATTHIREDB AACCGTGGAATCTCCGCTTGTGCTGTTTGGCAGCGAGCTGCTCCGATATTCGGTAAACAAA

490 500 510 520 530 540  
TR CCTCTTGGCGGTGATCGGTGGAGGCGATTCTGCAATGGAAGAAGCAAACTTTCTTACAAA  
ATTHIREDB CCTCTTGGCGGTGATCGGTGGAGGCGATTCTGCAATGGAAGAAGCAAACTTTCTTACAAA

550 560 570 580 590 600  
TR TATGGATCTAAAGTGTAATAATC[ATAGGAGAGATGCTTTTAGAGCGTCTAAGATTATG  
ATTHIREDB TATGGATCTAAAGTGTAATAATC[ATAGGAGAGATGCTTTTAGAGCGTCTAAGATTATG

610 620 630 640 650 660  
TR CAGCAGCGAGCTTTGTCTAATCCTAAGATTGATGTGATTTGGAACCTCGTCTGTTGTGGAA  
ATTHIREDB CAGCAGCGAGCTTTGTCTAATCCTAAGATTGATGTGATTTGGAACCTCGTCTGTTGTGGAA

670 680 690 700 710 720  
TR GCTTATGGAGATGGAGAAAGAGATGTGCTTGGAGGATTGAAAGTGAAAGATGTGGTTACC  
ATTHIREDB GCTTATGGAGATGGAGAAAGAGATGTGCTTGGAGGATTGAAAGTGAAAGATGTGGTTACC

730 740 750 760 770 780  
TR GGAGATGTTTTCTGATTTAAAAGTTTCTGGATTGTTCTTTGCTATTGGTCATGAGCCAGCT  
ATTHIREDB GGAGATGTTTTCTGATTTAAAAGTTTCTGGATTGTTCTTTGCTATTGGTCATGAGCCAGCT

790 800 810 820 830 840  
TR ACCAAGTTTTTTGGATGGTGGTGTTGAGTTAGATTCCGATGGTTATGTTGTCACGAAGCCT  
ATTHIREDB ACCAAGTTTTTTGGATGGTGGTGTTGAGTTAGATTCCGATGGTTATGTTGTCACGAAGCCT

850 860 870 880 890 900  
TR GGTACTACACAGACTAGCGTTCCCGGAGTTTTTCGCTGCGGGTGATGTTTCAGGATAAGAAAG  
ATTHIREDB GGTACTACACAGACTAGCGTTCCCGGAGTTTTTCGCTGCGGGTGATGTTTCAGGATAAGAAAG

910 920 930 940 950 960  
TR TATAGGCAAGCCATCACTGCTGCGAGGAAGTGGGTGCATGGCAGCTTTGGATGCGAGAGCAT  
ATTHIREDB TATAGGCAAGCCATCACTGCTGCGAGGAAGTGGGTGCATGGCAGCTTTGGATGCGAGAGCAT

970 980 990 1000 1010 1020  
TR TACTTACAAGAGATTGGATCTCAGCAAGGTAAGAGTGATTGA  
ATTHIREDB TACTTACAAGAGATTGGATCTCAGCAAGGTAAGAGTGATTGA

FIG. 1

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Translation of ATTHIREDB	10	20	30	40	50	60
Translation of TR	M N G L E T H N T R L C I V G S G P A A H T A A I Y A A R A E L K P L L F E G W M A N D I A P G G Q L N Q P P - R E N F					
Translation of ATTHIREDB	70	80	90	100	110	120
Translation of TR	P G F P E G I L G V E L T D K F R K Q S E R F G T T I F T E T V T K V D F S S K P F K L F T D S K A I L A D A V I L A I					
Translation of ATTHIREDB	130	140	150	160	170	180
Translation of TR	G A V A K W L S F V G S G E V L G G L W N R G I S A C A V C D G A A P I F R N K P L A V I G G G D S A M E E A N F L T K					
Translation of ATTHIREDB	190	200	210	220	230	240
Translation of TR	Y G S K V Y I I D I R R D A F R A S K I M Q Q R A L S N P K I D V I W N S S V Y E A Y G D G G E R D V L G G L K V K N V V T					
Translation of ATTHIREDB	250	260	270	280	290	300
Translation of TR	G D V S D L K V S G L F F A I G H E P A T K F L D G G V E L D S D G Y V V T K P G T T Q T S V P G V F A A G D V Q D K K					
Translation of ATTHIREDB	310	320	330	340	350	360
Translation of TR	Y R Q A I T A A G T G C M A A L D A E H Y L Q E I G S Q Q G K S D					

FIG. 2

Title: METHODS FOR THE PRODUCTION OF REDOX PROTEINS.

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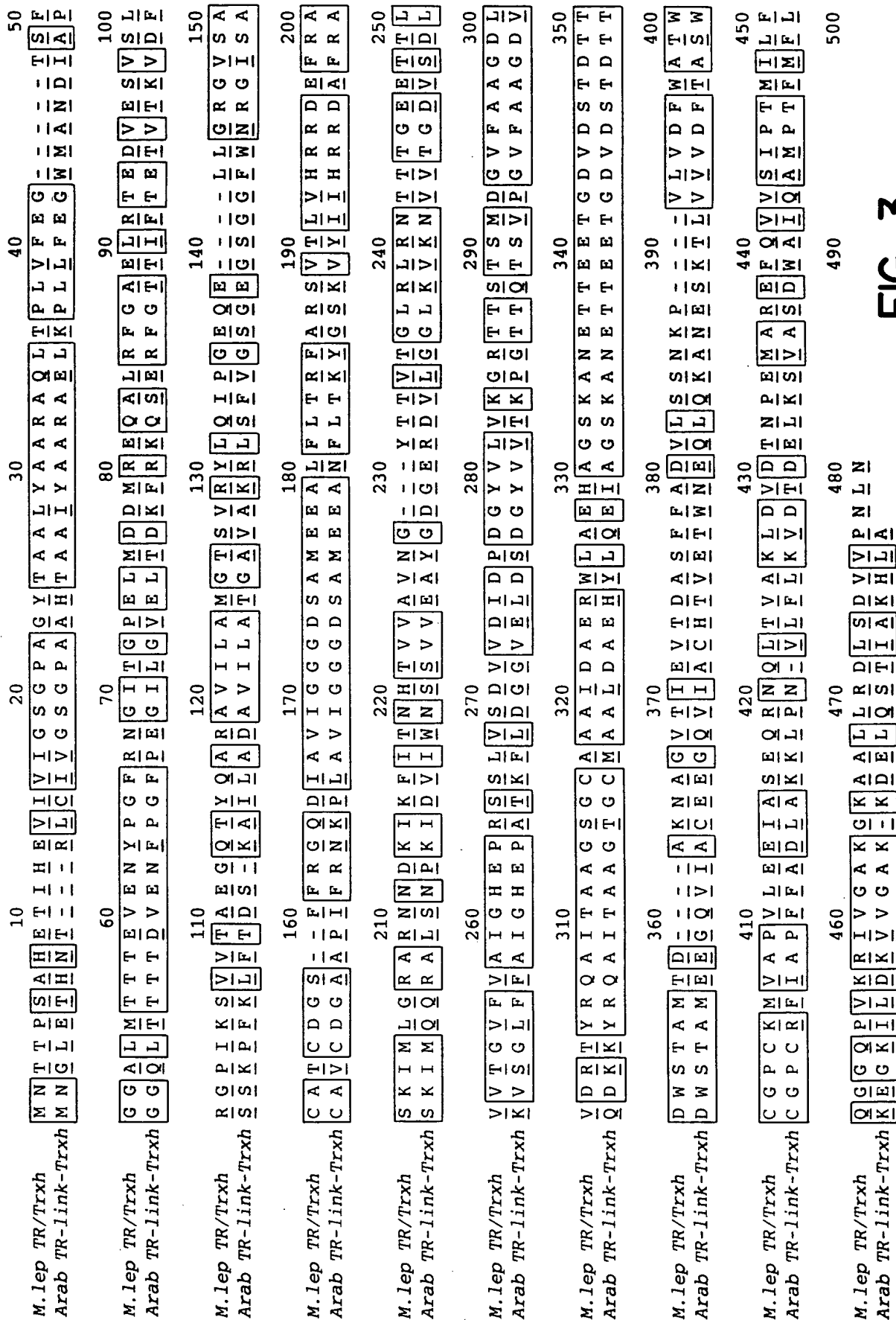


FIG. 3

DTNB Assay Summary

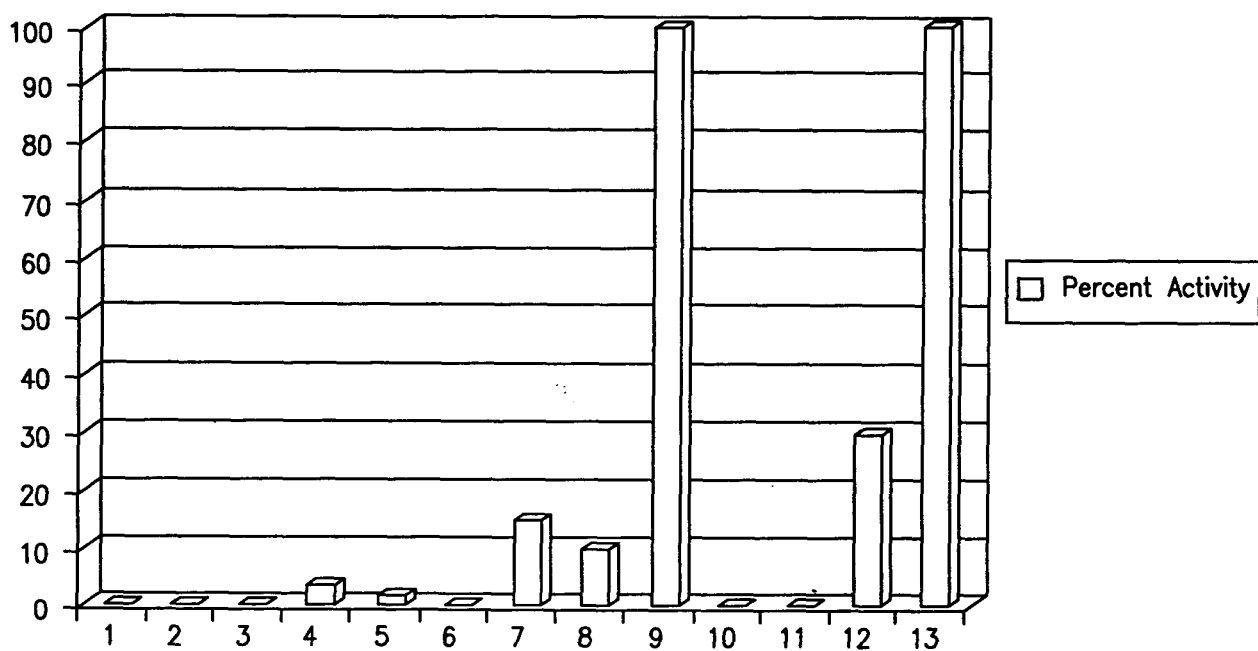


FIG. 4

# HETEROMULTIMERS

Class	Heteromultimer	Example sequence reference for heteromultimeric subunits
Biosynthetic	3-methyl-2-oxobutanoate dehydrogenase (2-oxoisovalerate dehydrogenase (lipoamide))- E1 component)	McKean, <i>et al.</i> Biochim. Biophys. Acta (1992) 1171:109-112 / Chuang, J.L., <i>et al.</i> FEBS Lett. a (1990) 262 (2), 305-309.
Biosynthetic	3-oxoadipate CoA-transferase	Parales, R.E. and Harwood, S.C. J. Bacteriol. (1992) 174:4657-4666
Biosynthetic	anthranilate synthase:indole-3-glycerol phosphate synthase	Zalkin, H.; <i>et al.</i> J. Biol. Chem. (1984) 259:3985-3992 .
Biosynthetic	beta-ketoacyl-[acyl carrier protein] synthase I	Siggaard-Andersen, M. <i>et al.</i> Proc. Natl. Acad. Sci. U.S.A. (1991) 88:4114-4118
Biosynthetic	butyrate--acetoacetate CoA-transferase	Fischer, R.J., <i>et al.</i> J. Bacteriol. (1993) 175 (21), 6959-6969.
Biosynthetic	cAMP dependent protein kinase	Mutzel, R <i>et al.</i> Proc. Natl. Acad. Sci. U.S.A. (1987) 84:6-10./ Burki, E., <i>et al.</i> Gene (1991) 102 (1), 57-65.
Biosynthetic	carbamoyl-phosphate synthase	Shigenobu, S., <i>et al.</i> Nature. (2000) 407 (6800), 81-86.
Biosynthetic	Creatine kinase	Billadello, J.J.; <i>et al.</i> Biochem. Biophys. Res. Commun. (1986) 138:392-398. / Roman, D.; <i>et al.</i> Proc. Natl. Acad. Sci. U.S.A. (1985) 82:8394-8398.
Biosynthetic	gamma-glutamyltransferase (gamma-glutamyl transpeptidase)	Papandrikopoulou, A.; <i>et al.</i> Eur. J. Biochem. (1989) 183:693-698.
Biosynthetic	glutathione transferase	Morrow, C.S. <i>et al.</i> Gene (1989) 75:3-11
Biosynthetic	glycerol-3-phosphate dehydrogenase	Cole, S.T. <i>et al.</i> J. Bacteriol. (1988) 170:2448-2456.
Biosynthetic	guanylate cyclase	Hinsch, K.D. <i>et al.</i> FEBS Lett. (1988) 239:29-34/ Koesling, D. <i>et al.</i> FEBS Lett. (1990) 266:128-132.
Biosynthetic	heterodisulfide reductase	Smith, D.R., <i>et al.</i> J. Bacteriol. (1997) 179 (22), 7135-7155.
Biosynthetic	human cathepsin	Ritonja, A. <i>et al.</i> FEBS Lett. (1988) 228:341-345.
Biosynthetic	Hydrogenase	Menon, N.K. <i>et al.</i> J. Bacteriol. (1990) 172:1969-1977.
Biosynthetic	Meprin A	Johnson, G.D. and Hersh, L.B. J. Biol. Chem. (1992) 267:13505-13512.
Biosynthetic	methionine adenosyltransferase	Horikawa, S.; Tsukada, K. FEBS Lett. (1992) 312:37-41.
Biosynthetic	methylmalonyl-CoA mutase	Jackson, C.A. <i>et al.</i> Gene (1995) 167:127-132.
Biosynthetic	mitochondrial processing peptidase	Pollock, R.A. <i>et al.</i> EMBO J. (1988) 7:3493-3500.
Biosynthetic	Na <sup>+</sup> /K <sup>+</sup> -exchanging ATPase	Shull, G.E., <i>et al.</i> Biochemistry (1986) 25 (25), 8125-8132./ Mercer, R.W., <i>et al.</i> Mol. Cell. Biol. (1986) 6 (11), 3884-3890./ Mercer, R.W., <i>et al.</i> J. Cell Biol. (1993) 121 (3), 579-586.
Biosynthetic	NAD(+)-dependent isocitrate dehydrogenase	Cupp, J.R. and McAlister-Henn, L. J. Biol. Chem. (1992) 267:16417-16423. /Cupp, J.R. and McAlister-Henn, L. J. Biol. Chem. (1991) 266:22199-22205.
Biosynthetic	phosphoribosylformylglycinamidine synthase	Ebbole, D.J.; Zalkin, H. J. Biol. Chem. (1987) 262:8274-8287.
Biosynthetic	protocatechuate 3,4-dioxygenase	Frazee, R.W.; <i>et al.</i> J. Bacteriol. (1993) 175:6194-6202.
Biosynthetic	S-100 protein	Engelkamp, D.; <i>et al.</i> Biochemistry (1992)

FIG. 5A

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		31:10258-10264. / Allore, R.J.; <i>et al.</i> J. Biol. Chem. (1990) 265:15537-15543.
Biosynthetic	sucrose--fructan 6-fructosyltransferase	Sprenger, N.; <i>et al.</i> Proc. Natl. Acad. Sci. U.S.A. (1995) 92:11652-11656.
Biosynthetic	Superoxide dismutase	Capo, C.R.; <i>et al.</i> Biochem. Biophys. Res. Commun. (1990) 173:1186-1193.
Biosynthetic	Urease	Labigne, A.; <i>et al.</i> J. Bacteriol. (1991) 173:1920-1931.
Biosynthetic	urokinase-type plasminogen activator (urokinase)	Belin, D. <i>et al.</i> Eur. J. Biochem. (1985) 148:225-232.
Biosynthetic	methylmalonyl-coenzyme A mutase	Birch, A.; <i>et al.</i> J. Bacteriol. (1993) 175 (11), 3511-3519.
Calcium binding	Calcineurin	Muramatsu, T. and Kincaid, R.L. Biochim. Biophys. Acta (1993) 1178 (1), 117-120 / Guerini, D. <i>et al.</i> DNA (1989) 8:675-682.
Calcium binding	Calgranulin	Imamichi, T. <i>et al.</i> Biochem. Biophys. Res. Commun. (1993) 194:819-825.
Calcium binding	Calpain	Aoki, K. <i>et al.</i> FEBS Lett. (1986) 205:313-317.
DNA binding	AP1	van Straaten, F.; <i>et al.</i> Proceedings of the National Academy of Sciences of the United States of America. (1983) 80 (11), 3183-3187. / Hattori, K.; <i>et al.</i> Proceedings of the National Academy of Sciences of the United States of America. (1988) 85 (23), 9148-9152.
DNA binding	cMyc-Max	Schreiber-Agus, N. <i>et al.</i> Mol. Cell. Biol. (1993) 13 (5), 2765-2775.
DNA binding	DNA binding protein HU-1/HU-2	Laine, B. <i>et al.</i> Eur. J. Biochem. (1980) 103:447-461.
DNA binding	hepatic nuclear factor 1	Bach, I. <i>et al.</i> Nucleic Acids Res. (1992) 20 (16), 4199-4204. / Rey-Campos, J. <i>et al.</i> EMBO J. (1991) 10 (6), 1445-1457.
DNA binding	Integration host factor	Miller, H.I. Cold Spring Harbor symposia on quantitative biology. (1984) 49, 691-698. / Flamm, E. and Weisberg, R.A. J. Mol. Biol. (1985) 183:117-128.
DNA binding	Ku	Reeves, W.H. and Stoecker, Z.M. J. Biol. Chem. (1989) 264 (9), 5047-5052. / J. Biol. Chem. (1989) 264 (23), 13407-13411.
DNA binding	MutS	Bocker <i>et al.</i> 1999. Cancer Research 59, 816-822.
DNA binding	NF-E2	Chan, J.Y. <i>et al.</i> Proc. Natl. Acad. Sci. U.S.A. (1993) 90 (23), 11366-11370. / Toki, T.; <i>et al.</i> Oncogene (1997) 14 (16), 1901-1910.
DNA binding	nuclear factor kB (NFkB)	Kieran M, <i>et al.</i> Cell. (1990) Sep 7;62(5):1007-18. / Ruben SM, <i>et al.</i> Science (1991) Mar 22;251(5000):1490-3. Erratum in: Science (1991) Oct 4;254(5028):11
Electron transport	corrinoid/iron-sulfur protein	Lu, W.P. <i>et al.</i> J. Biol. Chem. (1993) 268:5605-5614.
Electron transport	cytochrome d ubiquinol oxidase	Green, G.N. <i>et al.</i> J. Biol. Chem. (1988) 263:13138-13143.
Electron transport	cytochrome-c3 hydrogenase	Menon, N.K. <i>et al.</i> J. Bacteriol. (1987) 169:5401-5407.
Electron transport	electron transfer flavoprotein	Finocchiaro, G. <i>et al.</i> Biol. Chem. (1988) 263:15773-15780. / Finocchiaro, G. <i>et al.</i> Eur. J. Biochem. (1993) 213:1003-1008.

FIG. 5B

Electron transport	xylene monooxygenase	Shaw, J.P. and Harayama, S. Eur. J. Biochem. (1992) 209:51-61. / Kasai, Y., <i>et al.</i> J. Bacteriol. (2001) 183 (22), 6662-6666.
Growth factor	hepatocyte growth factor	Nakamura, T. <i>et al.</i> Nature (1989) 342:440-443.
Growth factor	human chorionic gonadotropin	Morgan, F.J. <i>et al.</i> J. Biol. Chem. (1975) 250 (13), 5247-5258.
Growth factor	Platelet-derived growth factor	Takimoto, Y., <i>et al.</i> Hiroshima J. Med. Sci. (1993) 42 (1), 47-52. / Josephs, S.F., <i>et al.</i> Science (1984) 225 (4662), 636-639.
Hormone	Bombyxin	Adachi, T. <i>et al.</i> J. Biol. Chem. (1989) 264:7681-7685.
Hormone	Follicle stimulating hormone	Fiddes, J.C. and Goodman, H.M. J. Mol. Appl. Genet. (1981) 1 (1), 3-18. / Watkins, P.C., <i>et al.</i> DNA (1987) 6 (3), 205-212.
Hormone	Insulin	Bell, G.I., Pictet, R.L., Rutter, W.J., Cordell, B., Tischer, E. and Goodman, H.M. Sequence of the human insulin gene. Nature. 284 (5751), 26-32 (1980)
Hormone	Luteinizing Hormone	Fiddes, J.C. and Goodman, H.M. J. Mol. Appl. Genet. (1981) 1 (1), 3-18. / Shome, B. and Parlow, A.F. J. Clin. Endocrinol. Metab. (1973) 36 (3), 618-621.
Hormone	Thyroid stimulating hormone	Fiddes, J.C. and Goodman, H.M. J. Mol. Appl. Genet. (1981) 1 (1), 3-18. / Hayashizaki Y, <i>et al.</i> FEBS Lett. (1985) 188 (2), 394-400.
Immune	B-cell antigen receptor complex	Hashimoto, S. <i>et al.</i> J. Immunol. (1993) 150 (2), 491-498. / Flaswinkel, H. and Reth, M. Immunogenetics (1992) 36 (4), 266-269.
Immune	Cell surface CD8 molecules	Ureta-Vidal, A., <i>et al.</i> Immunogenetics (1999) 49 (7-8), 718-721.
Immune	human complement subcomponent C1q	Sellar, G.C. <i>et al.</i> Biochem. J. (1991) 274:481-490.
Immune	T cell receptor	Talken, B.L. <i>et al.</i> Scand. J. Immunol. (2001) 54 (1-2), 204-210.
Photosynthesis	C-phycocyanin	Offner, G.D. <i>et al.</i> J. Biol. Chem. (1981) 256:12167-12175. / Troxler, R.F. <i>et al.</i> J. Biol. Chem. (1981) 256:12176-12184.
Photosynthesis	ferredoxin-thioredoxin reductase	Chow, L.P. <i>et al.</i> Eur. J. Biochem. (1995) 231:149-156. / Iwadate, H. <i>et al.</i> Eur. J. Biochem. (1994) 223:465-471.
Photosynthesis	Light harvesting complex I	Proc. Natl. Acad. Sci. U.S.A. (1984) 81, 189-192.
Photosynthetic	cytochrome b559	Carrillo, N. <i>et al.</i> Curr Genet. 1986;10(8):619-24.
Protease	ATP-dependent Clp protease	Gerth, U. <i>et al.</i> Gene (1996) 181:77-83. / Kunst, F. <i>et al.</i> Nature (1997) 390 (6657), 249-256.
Receptor	alpha-2-macroglobulin receptor	Strickland, D.K. <i>et al.</i> J. Biol. Chem. (1990) 265:17401-17404. / Strickland, D.K. <i>et al.</i> J. Biol. Chem. (1991) 266:13364-13369.
Receptor	Interleukin-2 receptor	Ishida, N. <i>et al.</i> Nucleic Acids Res. (1985) 13:7579-7589. / Hatakeyama, M. <i>et al.</i> Science (1989) 244:551-556 / Takeshita, T. <i>et al.</i> Science (1992) 257:379-382.
Receptor	platelet-derived growth factor receptor	Lee, K.H. <i>et al.</i> Mol. Cell. Biol. (1990) 10:2237-2246. / Herren, B. <i>et al.</i> Biochim. Biophys. Acta 1173 (3), 294-302 (1993).
Structural	Hemoglobin	Heindell, H.C. <i>et al.</i> Cell (1978) 15 (1), 43-54. /

FIG. 5C

		Best, J.S. <i>et al.</i> Hoppe-Seyler's Z. Physiol. Chem. (1989) 350 (5), 563-580. / Hardison, R.C. J. Biol. Chem. (1981) 256 (22), 11780-11786.
Structural	human platelet glycoprotein Ib	Wenger, R.H. <i>et al.</i> Biochem. Biophys. Res. Commun. (1988) 156 (1), 389-395. / Yagi, M. <i>et al.</i> J. Biol. Chem. (1994) 269 (26), 17424-17427.
Structural	Plasma fibronectin	Kornblihtt, A.R. <i>et al.</i> Proc. Natl. Acad. Sci. U.S.A. (1983) 80:3218-3222.
Structural	Spectrin	Sahr, K.E. <i>et al.</i> J. Biol. Chem. (1990) 265:4434-4443. / Winkelmann, J.C. <i>et al.</i> J. Biol. Chem. (1990) 265:11827-11832.
Structural	Tubulin	Ponstingl, H. <i>et al.</i> Proc. Natl. Acad. Sci. U.S.A. (1981) 78:2757-2761. / Krauhs, E. <i>et al.</i> Proc. Natl. Acad. Sci. U.S.A. (1981) 78:4156-4160.
Toxin	Agkisacutacin	Cheng, X. <i>et al.</i> Biochem. Biophys. Res. Commun. (1999) 265 (2), 530-535.
Toxin	Beta bungarotoxins	Kondo, K. <i>et al.</i> J. Biochem. (1978) 83:101-115.
Toxin	Crotoxin	Bouchier, C. <i>et al.</i> Nucleic Acids Res. (1988) 16 (18), 9050.
Toxin	Mojave toxin	John, T.R. <i>et al.</i> Gene (1994) 139:229-234.
Toxin	venom protein C9S3	Rowan, E.G. <i>et al.</i> Nucleic Acids Res. (1990) 18:1639. / Joubert, F.J. and Viljoen, C.C. Hoppe-Seyler's Z. Physiol. Chem. (1979) 360:1075-1090.
Miscellaneous	Inhibin	Forage, R.G. <i>et al.</i> Proc. Natl. Acad. Sci. U.S.A. (1986) 83:3091-3095.
Miscellaneous	Monellin	Frank, G. and Zuber, H. Hoppe-Seyler's Z. Physiol. Chem. (1976) 357:585-592.
Miscellaneous	mRNA capping enzyme	Niles, E.G. <i>et al.</i> , J. Virology (1986) 153:96-112.
Miscellaneous	Soybean insulin-binding protein si30	Barbashov, S.F. <i>et al.</i> Bioorg. Khim. (1991) 17:421-423.

FIG. 5D